IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	Garaci et al.	Confirmation No.: 9693
Serial No. :	10/533,942	
Filed :	May 4, 2005	
Art Unit :	1628	
Examiner :	Zareck, P.E.	
For :	**USE OF RESVERATROL FOR THE PREPARATION OF A MEDICAMENT USEFUL FOR THE TREATMENT OF INFLUENZA VIRUS INFECTION**	

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Commissioner for Patents
Alexandria, VA 22313-1450

APPEAL BRIEF UNDER 37 C.F.R. §41.37

This is an appeal from the rejection of claims 4-9 and 13-18 made in the Non-Final Office Action issued on November 26, 2010 in the referenced application ("Office Action"). For the reasons discussed below, Appellants request reversal of the rejections of the claims and allowance thereof.

A Notice of Appeal was filed on February 23, 2011, making the filing of this Appeal Brief timely.

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I. REAL PARTY IN INTEREST

The real party in interest is **Sigma-Tau Industrie Farmaceutiche Riunite S.P.A.** of Rome, Italy, the assignee of record.

II. RELATED APPEALS AND INTERFERENCES

None.

III. STATUS OF THE CLAIMS

Claims 4-9 and 13-18 are currently rejected and are presented on appeal.

Claims 1-3 and 10-12 have been previously cancelled.

A copy of the claims presented on appeal is attached in Section VIII, Claims Appendix.

IV. STATUS OF THE AMENDMENTS

No amendments have been filed subsequent to the Non-Final Office Action of November 26, 2010.

V. SUMMARY OF THE CLAIMED SUBJECT MATTER

Independent claim 4 recites a method of inhibiting influenza virus replication by administering to a subject in need an amount of resveratrol which inhibits influenza virus replication without inhibiting influenza virus target cell entry.

Support for independent claim 4, as pending, is found from page 8 line 23, to page 9 line 14, and on figures 3, 4A and 4B of the specification as originally filed.

Independent claim 7 recites a method of treating influenza virus infection by administering to a subject in need an amount of resveratrol which inhibits influenza virus replication without inhibiting influenza virus target cell entry.

Support for independent claim 7, as pending, is found on page 16, lines 6-17 and on figure 9 of the specification as originally filed.

Independent claim 13 recites a method of non-reversibly inhibiting influenza virus replication by administering to a subject in need an amount of resveratrol which inhibits influenza virus replication without inhibiting influenza virus target cell entry.

Support for independent claim 13, as pending, is found from page 8 line 23, to page 9 line 14, and on figures 3, 4A and 4B of the specification as originally filed.

Independent claim 16 recites a method of treating an influenza virus infection by administering to a subject in need an amount of resveratrol which non-reversibly inhibits influenza virus replication without inhibiting virus target cell entry.

Support for independent claim 16, as pending, is found from page 8, line 23, to page 9 line 14, page 16, lines 6-17 and on figures 3, 4A and 4B and 9 of the specification as originally filed.

VI. GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

A) Whether claims 4-9 and 13-18 are unpatentable under 35 U.S.C. § 103(a) over Root et al. (Journal of General Virology, 2000, hereinafter "Root") in view of Stewart et al. (Biochemistry, 1999 "Stewart") and Heredia et al. (Journal of Acquired Immune Deficiency Syndrome, 2000, hereinafter "Heredia").

B) Whether claims 4-9 and 13-18 are unpatentable under 35 U.S.C. § 112, ¶ 1, for failing to comply with the written description requirement.

VII. ARGUMENT

A) Rejection of Claims 4-9 and 13-18 over Root in View of Stewart and Heredia

Pending claims 4-9 and 13-18 were rejected under 35 U.S.C. § 103(a), for allegedly being unpatentable over Root in view of Stewart and Heredia (Office Action, page 4).

Appellants discuss below the errors made by the Examiner and how, in view of these errors, the claims do contain subject matter which would not have been rendered obvious by the combination of the cited references.

Independent claims 4, 7, 13 and 16 are generally directed to a method of inhibiting the replication of influenza virus or to a method of treating an influenza virus infection by administering an effective amount of resveratrol. This amount of resveratrol is capable of inhibiting the virus replication without inhibiting the viral entry into the target cells. The antiviral activity of resveratrol is not reversible upon discontinuation of the treatment (*e.g.*, specification, from page 8, line 23, to page 9 line 14, page 16, lines 6-17 and figures 3, 4A and 4B and 9).

Root does not disclose Appellants' invention. Root only provides for a PKC inhibitor, bisindolylmaleimide I.HCL, which reversibly inhibits viral cell entry (*e.g.*, page 2701, lines 10-13, 14-17 and 48-51 and page 2699, right col, lines 46-49). Accordingly, Root does not disclose a method for non-reversibly inhibiting influenza virus replication without inhibiting influenza virus target cell entry. Thus, Root does not disclose all of the claimed limitations.

Stewart does not correct Root's deficiencies nor does it disclose Appellants' invention. Stewart only provides for the anti-cancer activity of resveratrol (*e.g.*, page

13244, col. 1, lines 3-4). Specifically, Stewart discloses that resveratrol is a cancer chemoprotective agent that antagonizes each stage of the carcinogenesis and that weakly inhibits protein kinase C (*e.g.*, page 13249, right col., lines 1-3 and 24-26).

Moreover, Stewart is completely silent with regard to methods of treating influenza virus infection or methods of inhibiting influenza virus replication as presently claimed. Accordingly, Stewart as well does not disclose all of the claimed limitations either alone or in combination with Root.

Heredia cannot make up for the deficiencies of the combination of Root with Stewart. Heredia describes that resveratrol, together with zidovudine synergistically inhibits HIV replication (*e.g.*, summary, lines 3-5). Heredia is also completely silent with regard to the presently claimed subject matter, that is, Heredia does not disclose a method of treating influenza virus infection or a method of inhibiting influenza virus replication comprising administering resveratrol in a dose that inhibits viral cell replication without inhibiting virus target cell entry.

Thus, none of the cited references, either alone or in combination, disclose all of the claimed subject matter. Therefore, the Examiner's comment of page 3, point 3 of the Office Action is irrelevant. The Examiner has taken the position that Applicants have not disagreed with Stewart or Heredia in the capacity in which they were applied to the instant claims (*e.g.*, that resveratrol inhibits PKC [Stewart] or the virtues of resveratrol (*e.g.*, low cost, established safety profile) [Heredia].

Appellants assert that the claims are not directed to a method of inhibiting PKC. The presently claimed subject matter is directed to a method of inhibiting influenza virus replication or treating an influenza virus infection by administering resveratrol in a dose

that inhibits viral cell replication without inhibiting virus target cell entry. The low cost and the established safety profile of resveratrol are not enough to provide the motivation to one skilled in the art to use a drug indicated as a cancer chemoprotective agent or as an HIV inhibitor to treat influenza virus infection.

None of the cited references, either alone or in combination disclose what is presently claimed. On the contrary, Root disclose the exact opposite, that is, that a PKC inhibitor irreversibly blocks (e.g., inhibits) virus cell entry. Thus, the Examiner's reasoning for maintaining the claim rejection is incorrect.

Moreover, Appellants respectfully disagree also with the Examiner's statement on page 3, point 4 of the Office Action.

The use of resveratrol for inhibiting influenza virus replication and for treating influenza virus infection is not rendered obvious by the teachings of Root which describes that PKC inhibits the virus replication by inhibiting its entry into the cells. The mechanism of resveratrol is not disclosed by Root which describes the PKC inhibitor bisindolylmaleimide. Moreover, Root does not suggest that all of the PKC shares the same mechanism. On the contrary, it describes that bisindolylmaleimide has a mechanism quite different from the PKC H7 (*e.g.*, page 2699, right col, lines 46-49).

Moreover, resveratrol does not reversibly block the virus from entry into the cells, but it inhibits the viral replication inside the cells.

Thus, a person skilled in the art would not consider treating influenza virus infection or inhibiting influenza virus replication with resveratrol by combining the teachings of Root with the teachings related to a cancer chemoprotective agent or to a

treatment to inhibit HIV replication as disclosed by Stewart and Heredia, respectively. These results are non-transferable to influenza virus infection.

Thus, for this additional reason, Appellants assert that Root, even if combined with Stewart and Heredia, would not have rendered obvious the claimed subject matter to one skilled in the art.

Finally, is also completely irrelevant that the dose described by Stewart corresponds to 3.4 μg. This dose cannot be a starting point to inhibit virus replication as stated by the Examiner (*e.g.*, page 4 of the Office Action) because a person skilled in the art, as submitted above, would not consider using resveratrol in the field of influenza virus by combining the teachings of Root, Stewart and Heredia.

Accordingly, the Examiner's conclusion that the art suggests using a dose of resveratrol that inhibits the replication but not the entry of the virus into the cells is incorrect and based on the impermissible hindsight.

Thus, for all of the reasons set forth above, Appellants respectfully submit that the combination of the cited references would not have rendered obvious the claimed subject matter to one skilled in the art and submit that the rejection of 4-9 and 13-18 under 35 U.S.C. § 103(a) is untenable and improper.

B) Rejection of Claims 4-9 and 13-18 33 for Failing to Comply with the Written Description Requirement

On page 5 of the Office Action, the Examiner has indicated that the amended claims contain new matter and that the specification fails to discuss at which doses resveratrol inhibits influenza virus replication without inhibiting target cell entry.

As an initial matter, the standard to satisfy the written description requirement is that a patent specification must describe the claimed invention in sufficient detail so that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention. *Moba, B.V. v. Diamond Automation, Inc.*, 325 F.3d 1306, 1319, 66 USPQ2d 1429, 1438 (Fed. Cir. 2003). Thus, the specification does not have to disclose, either implicitly or explicitly that only specific doses of resveratrol inhibit influenza virus replication without inhibiting the virus target cell entry.

The specification discloses that a dose of 20 μg/ml of resveratrol is capable of inhibiting the virus replication but not the target cell entry. Thus, it sufficiently shows to those skilled in the art that the Appellants were in possession of the claimed invention.

Further, the claim should not be rejected or objected to on the ground of new matter. *In re Rasmussen*, 650 F.2d 1212, 211 USPQ 323 (CCPA 1981).

The concept of new matter is properly employed as a basis for objection to amendments, abstract, specification, claims or drawings attempting to add new disclosure to that originally presented. However, information contained in any one of the specification, claims or drawing of the application as filed may be added to any other part of the application without introducing new matter.

Appellants respectfully submit that the specification fully support the notion that resveratrol does not inhibit the entry of the virus into the cells, but it inhibits the viral replication (*e.g.*, page 8, line 23 page 10 line 18, figures 3, 4A, 4B, 7A and 7B). Thus, it fully supports the presently claimed subject matter.

Moreover, a description as filed is presumed to be adequate, unless or until sufficient evidence or reasoning to the contrary has been presented by the examiner to rebut the presumption. *In re Marzocchi*, 439 F.2d 220, 224, 169 USPQ 367, 370 (CCPA 1971). In other words, the examiner has the initial burden of presenting by a preponderance of evidence why a person skilled in the art would not recognize in an applicant's disclosure a description of the invention defined by the claims. *In re Wertheim*, 541 F.2d 257, 191 USPQ 90 (CCPA 1976). Appellants respectfully submit that the Examiner has not met his burden. The specification discloses that 20 μg/ml of resveratrol are capable of inhibiting influenza virus replication without affecting the entry of the virus into a target cell. Appellants are not required to show different ranges of resveratrol to prove this irrefutable effect. Thus, for all of these reasons, Appellants respectfully submit that the claims comply with the written description requirement because they contain subject matter described in the specification in such a way as to reasonably convey to one skilled in the art that the inventor had possession of the claimed invention at the time the application was filed.

Accordingly, it is respectfully submitted that the rejection of claims 4-9 and 13-18 under 35 U.S.C. § 112, ¶ 1, is untenable and improper.

VIII. CLAIMS APPENDIX

4. A method of inhibiting influenza virus replication comprising administering to a subject having an influenza virus infection an amount of resveratrol which inhibits influenza virus replication and does not inhibit influenza virus target cell entry.

5. The method of claim 4 wherein the subject is a human and the influenza virus is human influenza virus.

6. The method of claim 4, wherein the influenza infection is a veterinary virus infection and the subject is a veterinary animal.

7. A method of treating an influenza virus infection comprising administering to a subject having an influenza infection an effective amount of resveratrol, which inhibits influenza virus replication and does not inhibit influenza virus target cell entry.

8. The method of claim 7 wherein the subject is a human and the influenza virus is a human influenza virus.

9. The method of claim 7 wherein the influenza virus is a veterinary virus infection and the subject is a veterinary animal.

13. A method of non-reversibly inhibiting influenza virus replication comprising administering to a subject having an influenza infection an amount of resveratrol which inhibits influenza virus replication and does not inhibit influenza virus target cell entry.

14. The method of claim 13 wherein the subject is a human and the influenza virus is human influenza virus.

15. The method of claim 13 wherein the influenza infection is a veterinary virus infection and the subject is a veterinary animal.

16. A method of treating an influenza virus infection comprising administering to a subject having an influenza infection an effective amount of resveratrol which non-reversibly inhibits influenza virus replication and does not inhibit influenza virus target cell entry.

17. The method of claim 16, wherein the subject is a human and the influenza virus is a human influenza virus.

18. The method of claim 16 wherein the influenza infection is a veterinary virus infection and the subject is a veterinary animal.

IX. EVIDENCE APPENDIX

None.

X. RELATED PROCEEDINGS APPENDIX

None.

FEES

Payment by credit card in the amount of Five Hundred Forty Dollars ($540.00) is being concurrently made with the filing of this paper to cover the fee set forth in 37 C.F.R. §41.20(b)(2) for a large entity.

It is believed that no fees other than those paid concurrently are due in connection with the filing of this paper. However, should it be deemed that any other fee is due in connection with this paper, authorization is hereby given to charge such fee to Deposit Account No. 02-2275.

Respectfully submitted

Date: April 21, 2011

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